

WHAT IS CLAIMED IS:

1. A method of characterizing a first molecule X and a second immobilized molecule Y in a sample of a conducting medium, said method comprising:
- 5 (a) providing a system comprising said immobilized second molecule Y, said conducting medium sample, and said first molecule X;
- (b) detecting a transient electrical signal produced by a monodirectional movement of said first molecule X through said conducting medium sample relative to said immobilized second molecule Y; and
- 10 (c) relating said detected transient electrical signal to at least one characterizing feature of said first molecule X and said second molecule Y in said sample.
2. The method according to Claim 1, wherein said at least one characterizing feature is motion, velocity, quantity, structure, charge or binding event.
- 15 3. The method according to Claim 1, wherein said movement is a movement of X towards Y.
4. The method according to Claim 1, wherein said movement is a movement of X away
- 20 from Y.
5. The method according to Claim 1, wherein said conducting medium sample is a fluid medium.
- 25 6. The method according to Claim 1, wherein said conducting medium sample is a gel or gaseous medium.
7. The method according to Claim 1, wherein said immobilized molecule Y is a polymer.
- 30 8. The method according to Claim 7, wherein said polymer is a polypeptide.
9. The method according to Claim 7, wherein said polymer is a nucleic acid.

10. The method according to Claim 1, wherein said immobilized second molecule Y is immobilized on a surface of a first working electrode.

5 11. The method according to Claim 10, wherein said transient electrical signal is measured using said first working electrode and a second reference electrode.

12. The method according to Claim 10, wherein said transient electrical signal is measured using a plurality of electrodes, which plurality includes said first working
10 electrode.

13. The method according to Claim 1, wherein said transient electrical signal is a change in an electrical parameter over time.

15 14. The method according to Claim 13, wherein said electrical parameter is voltage.

15. The method according to Claim 13, wherein said electrical parameter is current.

16. The method according to Claim 13, wherein said electrical parameter is
20 accumulated charge.

17. The method according to Claim 13, wherein said electrical parameter is impedance of said medium.

25 18. A method according to Claim 1, wherein said second immobilized molecule Y is a polymer immobilized on a surface of a working electrode, said conducting medium sample is fluid medium; said transient electrical signal is measured using said first working electrode and a second reference electrode; said movement is a movement of X towards Y; and said at least one characterizing feature is a binding event between X and Y.

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19. The method according to Claim 18, wherein said immobilized polymer is a polypeptide.

20. The method according to Claim 19, wherein said first molecule X is a polypeptide.

21. The method according to Claim 19, wherein X and Y are proteins.

5 22. The method according to Claim 21, wherein X and Y are a receptor-ligand pair.

23. The method according to Claim 21, wherein X and Y are an antibody-antigen pair.

24. The method according to Claim 18, wherein said immobilized polymer is a nucleic
10 acid.

25. The method according to Claim 24, wherein said first molecule X is a nucleic acid.

26. The method according to Claim 24, wherein said first molecule X is a nucleotide.

15 27. The method according to Claim 26, wherein said method is a method of detecting
the covalent bonding of a nucleotide to a 3' end of a primer containing nucleic acid via a
polymerase catalyzed template dependent primer extension reaction.

20 28. The method according to Claim 24, wherein said method is a method of sequencing
a nucleic acid.

29. The method according to Claim 24, wherein said method is a method of detecting a
nucleic acid analyte in a sample.

25 30. The method according to Claim 29, wherein said nucleic acid analyte comprises a
SNP.

31. The method according to Claim 29, wherein said method quantitatively determines
30 the amount of said nucleic acid analyte in said sample.

32. The method according to Claim 31, wherein said method is a method of gene
expression profiling.

33. The method according to Claim 26, wherein said method is a PCR method.

34. A method of detecting the occurrence of a polymerase mediated template
5 dependent primer extension reaction in a medium, said method comprising:
 (a) providing a system comprising an immobilized template primer duplex
 nucleic acid made up of template and primer nucleic acids in contact with said
 medium, wherein said medium comprises a polymerase and at least one nucleotide;
 (b) detecting a transient electrical signal produced in said medium by covalent
10 bonding of said at least one nucleotide to a terminus of said primer nucleic acid; and
 (c) relating said detected transient electrical signal to the occurrence of a
 polymerase mediated template dependent primer extension reaction in said
 medium.

15 35. The method according to Claim 34, wherein said transient electrical signal is a
change in an electrical parameter over time.

36. The method according to Claim 35, wherein said detected polymerase mediated
template dependent primer extension reaction is the covalent addition of at least one
20 nucleotide to said primer nucleic acid's 3' end.

37. The method according to Claim 33, wherein said duplex nucleic acid is immobilized
on a surface of a first working electrode.

25 38. The method according to Claim 37, wherein said transient electrical signal is
measured using said first working electrode and a second reference electrode.

39. The method according to Claim 37, wherein said transient electrical signal is
measured using a plurality of electrodes, which plurality includes said first working
30 electrode.

40. The method according to Claim 33, wherein said medium is an aqueous fluid
medium.

41. The method according to Claim 33, wherein said medium comprises only one type of nucleotide.

5 42. The method according to Claim 33, wherein said medium comprises at least two different types of nucleotides.

43. The method according to Claim 42, wherein said medium comprises ATP, GTP, CTP and TTP.

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44. The method according to Claim 33, wherein said method is a method of sequencing a nucleic acid.

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45. The method according to Claim 33, wherein said method is a method of detecting a nucleic acid analyte and said method further comprises relating the occurrence of a polymerase mediated template dependent primer extension reaction to the presence of said nucleic acid analyte in said medium.

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46. The method according to Claim 45, wherein said nucleic acid analyte is a SNP.

47. The method according to Claim 45, wherein said nucleic acid analyte is a nucleic acid from a pathogenic organism.

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48. The method according to Claim 33, wherein said method is a method of gene expression profiling.

49. The method according to Claim 33, wherein said method is a method of monitoring a PCR reaction in real time.

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50. A method of sequencing a nucleic acid, said method comprising:
(a) providing a system comprising an immobilized template primer duplex nucleic acid made up of said nucleic acid hybridized to a primer nucleic acid, wherein said immobilized template primer duplex nucleic acid is immobilized on a

surface of a working electrode and is in contact with a medium comprising a polymerase and at least one nucleotide;

(b) detecting a transient electrical signal produced in said medium by covalent bonding of said at least one nucleotide to a terminus of said template nucleic acid; and

(c) determining said sequence of said nucleic acid using said detected transient electrical signal.

51. The method according to Claim 50, wherein said method comprises producing said template primer duplex nucleic acid and then immobilizing said duplex nucleic acid.

52. The method according to Claim 50, wherein said method comprises immobilizing said template nucleic acid followed by hybridization of said immobilized template nucleic acid to said primer nucleic acid.

53. The method according to Claim 50, wherein said method comprises immobilizing said primer nucleic acid followed by hybridization of said immobilized primer nucleic acid to said template nucleic acid.

54. The method according to Claim 50, wherein said medium comprises a single type of nucleotide and said method comprises two or more iterations of said steps (a) and (b) to produce a plurality of transient electrical signals from which said sequence of said nucleic acid is determined.

55. The method according to Claim 50, wherein said medium comprises at least two different nucleotides.

56. The method according to Claim 55, wherein said medium comprises GTP, ATP, CTP and TTP and said determining step comprises reading said sequence from a single detected transient electrical signal.

57. A method of detecting the occurrence of a binding event between a first molecule and an immobilized second molecule in a medium, said method comprising:

- (a) providing a system comprising said immobilized second molecule immobilized on a surface of a working electrode and in contact with a medium comprising said first molecule;
- (b) detecting a transient electrical signal in said medium produced by a binding event between said first molecule said immobilized second molecule; and
- (c) relating said detected transient electrical signal to the occurrence of said binding event between said first and second molecule.

58. The method according to Claim 57, wherein first and second molecules are proteins.

59. The method according to Claim 57, wherein said first and second molecules are a receptor-ligand pair.

60. The method according to Claim 57, wherein said first and second molecules are an antibody-antigen pair.

61. The method according to Claim 57, wherein said first and second molecules are nucleic acids.

62. An apparatus comprising:

- (a) a medium containment element containing a medium having a first molecule;
- (b) a working electrode having a second molecule immobilized on a surface thereof, wherein said surface is in contact with said medium;
- (c) a driver to drive said working electrode; and
- (e) a signal processor to obtain a response of said first and to generate a transient electrical signal based thereon.

63. The apparatus according to Claim 62, wherein said apparatus further comprises a reference electrode in contact with said medium and said signal processor compares responses from said working and reference electrode to generate said transient electrical signal.

64. The apparatus according to Claim 63, wherein said driver comprises a differential amplifier to create a charge difference between said electrodes in said medium.

65. The apparatus according to Claim 63, wherein said working and reference electrodes are present on a planar surface of a semiconductor substrate.

- 5 66. A device for use in practicing the method of Claim 1, said device comprising:
- (a) a transient electrical signal detection element for detecting a transient electrical signal caused by movement of said first molecule X through a conducting medium sample relative to said immobilized second molecule Y; and
 - (b) a computer readable medium on which is recorded an algorithm that relates
- 10 said transient electrical signal generated by said movement of said first molecule X relative to said immobilized second molecule Y to at least one characterizing feature of said first molecule X and said second molecule Y in said sample.

15 67. The device according to Claim 66, wherein said at least one characterizing feature is motion, velocity, quantity, structure, charge or binding event.

68. The device according to Claim 66, wherein said at least one characterizing feature is a binding event between said first molecule X and said second molecule Y.

20 69. The device according to Claim 66, wherein said transient electrical signal detection element comprises at least one working electrode.

70. The device according to Claim 69, wherein said transient electrical signal detection element comprises said at least one working electrode and a reference electrode.

25 71. The device according to Claim 69, wherein said transient electrical signal detection element comprises a plurality of electrodes, one of which is said at least one working electrode.

30 72. The device according to Claim 66, wherein said device further comprises a differential amplifier.

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73. The device according to Claim 72, wherein said differential amplifier is a differential voltage amplifier.
74. The device according to Claim 72, wherein said differential amplifier is a differential current amplifier.
75. The device according to Claim 66, wherein said device further includes a sample containment element.
76. The device according to Claim 75, wherein said device is an integrated device.
77. The device according to Claim 75, wherein said device comprises at least two distinct sample containment means each having its one transient electrical signal detection element.
78. The device according to Claim 77, wherein said device has a chip configuration.
79. The device according to Claim 77, wherein said device has an array configuration.
80. The device according to Claim 66, wherein said immobilized second molecule Y is a polymer.
81. The device according to Claim 80, wherein said polymer is immobilized on a surface of a working electrode component of said transient electrical signal detection element.
82. The device according to Claim 81, wherein said polymer is a polypeptide.
83. The device according to Claim 81, wherein said polymer is a nucleic acid.
84. A system for use in practicing the method of Claim 1, wherein said system comprises:

(a) a transient electrical signal detection element for detecting a transient electrical signal caused by movement of a first molecule X through a conducting medium sample relative to immobilized second molecule Y;

(b) an algorithm present on a computer readable medium that relates said transient electrical signal generated by said movement of said first molecule X relative to said immobilized second molecule Y to at least one characterizing feature of said first molecule X and said second molecule Y in said sample; and

(c) a conducting medium sample comprising first molecule X in contact with said immobilized second molecule Y.

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85. The system according to Claim 84, wherein said at least one characterizing feature is motion, velocity, quantity, structure, charge or binding event.

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86. The system according to Claim 84, wherein said at least one characterizing feature is a binding event between said first molecule X and said second molecule Y.

87. The system according to Claim 84, wherein said conducting medium sample is a fluid medium.

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88. The system according to Claim 84, wherein said conducting medium sample is a gel or a gaseous medium.

89. The system according to Claim 84, wherein said transient electrical signal detection element comprises at least one working electrode.

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90. The system according to Claim 89, wherein said transient electrical signal detection element further comprises a reference electrode.

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91. The system according to Claim 89, wherein said transient electrical signal detection element comprises a plurality of electrodes, wherein said plurality comprises said at least one working electrode.

92. The system according to Claim 84, wherein said system further comprises a differential amplifier.

93. The system according to Claim 92, wherein said differential amplifier is a differential voltage amplifier.

5 94. The system according to Claim 92, wherein said differential amplifier is a differential current amplifier.

95. The system according to Claim 84, wherein said immobilized second molecule Y is a polymer.

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96. The system according to Claim 95, wherein said polymer is a polypeptide.

97. The system according to Claim 95, wherein said polymer is a nucleic acid.

15 98. A computer readable medium on which is recorded an algorithm for relating a transient electrical signal caused by movement of a first molecule X through a conducting medium relative to second immobilized molecule Y to at least one characterizing feature of said first molecule X and said second molecule Y in said medium.

20 99. The computer readable medium according to Claim 98, wherein said at least one characterizing feature is motion, velocity, quantity, structure, charge or binding event.

100. The computer readable medium according to Claim 99, wherein said at least one characterizing feature is a binding event between said first molecule X and said second molecule Y.

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101. The computer readable medium according to Claim 98, wherein said second immobilized molecule Y is a polymer.

30 102. The computer readable medium according to Claim 101, wherein said polymer is a polypeptide.

103. The computer readable medium according to Claim 102, wherein said first molecule X is a polypeptide.

5 104. The computer readable medium according to Claim 101, wherein said polymer is a nucleic acid.

105. The computer readable medium according to Claim 104, wherein said first molecule X is a nucleic acid.

10 106. The computer readable medium according to Claim 104, wherein said first molecule X is a nucleotide.

15 107. The computer readable medium according to Claim 106, wherein said algorithm provides the identity of said nucleotide.

108. The computer readable medium according to Claim 106, wherein said algorithm provides the sequence of said immobilized nucleic acid.

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